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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/845,042	04/27/2001	Filippo Belardelli	B-4161 618742-8	1462

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Richard P. Berg, Esq
c/o LADAS & PARRY
Suite 2100
5670 Wilshire Boulevard
Los Angeles, CA 90036-5679

EXAMINER	
EWOLDT, GERALD R	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 12/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/845,042	BELARDELLI ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *28 June 2004* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *54-71* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *54-71* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's amendments and remarks, filed 6/28/04, are acknowledged.

2. Applicant has canceled all pending claims and substituted new Claims 54-71, all of which read on the elected invention and are being acted upon. In view of said substitution, all previous rejections under the second paragraph of 35 U.S.C. 112 have been withdrawn. In view of the new limitation excluding the inclusion of IL-4 in the claimed culture process, the previous rejections under 35 U.S.C. 102(b) as being anticipated by Bartholome et al. have also been withdrawn.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 54-70 stand rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. Elements critical or essential to the practice of the invention, but not included in the claims are not enabled by the disclosure, for the reasons of record set forth in the action mailed 1/28/04.

Briefly, the specification discloses that *only* cultures employing 1000 IU/ml IFN resulted in functional DCs. Accordingly, the use of 1000 IU/ml IFN in the claimed method would be considered essential to the instant invention. Likewise, *all* disclosed cultures employed 500 IU/ml GM-CSF. Thus, the use of 500 IU/ml GM-CSF in the claimed method would also be considered essential to the instant invention.

Applicant's arguments, filed 6/28/04, have been fully considered but they are not persuasive. Applicant argues that a person skilled in the art would understand that the claimed method would function with any concentration of type I IFN greater than 100 IU/ml, however, the claims have been amended to recite a minimum concentration of type I IFN greater than 400 IU/ml.

It remains the Examiner's position that it was Applicant's decision to disclose the use of just a single concentration of IFN and a single concentration of GM-CSF. Like the skilled

artisan referred to in Applicant's arguments, Applicant could easily have demonstrated that a range of cytokine concentrations (commensurate in scope with that of the claims) could function in the claimed method. Note that in particular, there is no evidence of record that DCs can be derived in a type I IFN alone (absent any GM-CSF) nor that a DC can be matured (presumably the object of adding the "maturation factor" of Claim 62) absent IL-4.

Applicant argues that a claimed invention is presumed enabling unless there is reason to doubt the objective truth thereof.

It is unclear to the Examiner just what "objective truth" Applicant's argument refers to. Both "objective" and "truth" imply the disclosure of some fact/data/reality. Applicant has provided only assertion which is considered neither "objective" nor "truth". Regarding the presumption of enablement, Applicant is advised that MPEP 2164.03 clearly states that physiological processes are generally considered to be unpredictable. Given this inherent unpredictability, an enabling disclosure commensurate in scope with the breadth of the claims is required. Mere assertion that an invention will work is simply inadequate when the invention encompasses a physiological process.

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 54-71 stand rejected under 35 U.S.C. 102(b) as being clearly anticipated by Paquette et al. (1998), for the reasons of record set forth in the action mailed 1/28/04.

Applicant's arguments, filed 6/28/04, have been fully considered but they are not persuasive. Applicant argues that "PAQUETTE et al. do not describe or suggest a process wherein type I IFN could mediate the differentiation of monocytes into differentiated dendritic cells as early as 3 days."

It is the Examiner's position that the method of the reference is the method of the instant claims. The reference teaches the culture of monocytes in IFN and GM-CSF. Note that said culture comprises the only actual step of the claimed

method. Applicant's further characterization of the results of performing this process does not now render the known process patentably distinct.

7. The following are new grounds for rejection necessitated by Applicant's amendment.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 54-62, 64, 68 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically:

A) Claim 54 is grammatically unclear in the recitation of "in culture within 3 days" as it is unclear what the within 3 days refers to.

B) Claim 55 is vague and indefinite as they recite a method employing "any synthetic type I IFN" as the term is not defined in the specification.

C) Claim 62 is vague and indefinite as they recite a method employing a "maturation agent" as the term is not defined in the specification.

D) Claim 64 is vague and indefinite as they recite a method employing a "growth factor" as the term is not defined in the specification.

E) In Claim 68, in line 3, PBMC and CD14+ monocytes should properly be PBMC or CD14+ monocytes.

Applicant has traversed rejections similar to B) and C), in the previous Office action. Regarding B), Applicant argues that the term is "given meaning" at page 6, lines 1-10 of the specification. Applicant further argues that several references that are not of record support the use of the term. Applicant asserts that "A person skilled in the art would understand that this phrase includes any synthetic type I IFN produced from recombinant DNA, including in particular synthetic consensus IFN (CIFN) whose sequence based on a consensus derived from amino acid sequences of human IFN-alpha. Therefore, applicants believe consider that this expression is definite to a person skilled in the art."

A review of the specification shows that no definition of the term is disclosed at page 6. Regarding the references that are not of record, said references have not been considered and

no comment can be offered on their content. Regarding Applicant's assertion regarding what a person skilled in the art would know, an attorney's assertions alone do not comprise a convincing argument.

Regarding C), Applicant argues, that at 2 newly submitted references provide an illustration of maturation agents. Applicant also argues that at page 4 of the specification it is disclosed that "further dendritic cell (DENDRITIC CELL) maturation can be driven by the addition of TNF-alpha, IL-1, LPS, monocyte-conditioned medium or sCD40L".

Applicant has not indicated where in the newly submitted references support for the instant assertions can be found. It is also noted that the newly submitted references have not been made of record. Accordingly, the references have not been found convincing. A review of page 4 of the specification reveals that the term "maturation agent" is not defined and no metes and bounds for the term are established. A disclosure of a means for "further maturation" of DCs does not define the term in question.

10. Claims 54-71 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A) A process ... with a Type I IFN concentration greater that 400 IU/ml (Claims 54 and 63).

B) A process ... in the absence of IL-4 (Claims 54, 63, 68) or wherein IL-4 is absent (Claim 69).

C) A process ... comprising adding a growth factor which promotes monocyte/dendritic cell survival (Claim 59).

Applicant has indicated that support for the new limitations can be found in the specification at pages 7 and 16. A review of the specification reveals no support for the new limitations. Note that examples found later in the specification in which IL-4 is absent are insufficient to support the generic method of the independent claims.

11. No claim is allowed.

12. Applicant's amendment or action necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

14. **Please Note:** Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see www.uspto.gov/ebc/newusers.html. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

10/15/04

G.R. Ewoldt, Ph.D.
Primary Examiner
Technology Center 1600

G.R. EWOLDT, PH.D.
PRIMARY EXAMINER